proteoliposomes (1 mg M2(22-62) in 20 mg POPE:POPC:POPG, 3:1:1). The 250-μm bilayer was estimated to contain $2.9x10^7$ tetramers. The channel conductance was undetectable with symmetrical pH 7.5 at −30 mV (*trans* relative to *cis*). Upon acidification of the *cis* chamber to pH 5.5 (and stirring), there was a smooth increase in current to a level of 633 pS (−19 pA, i.e. current flow from *cis* to *trans*, 4.1 protons/tetramer/s). Then, amantadine was injected *cis* and *trans* to a concentration of 0.1 mM. Stirring *cis* produced 79% block over the course of 5.6 minutes. The residual current was constant for the next 5.6 min. Then, *cis* neutralization eliminated the residual current. Rechallenge with *cis* acidification (with amantadine present) showed persistence of block. Acidification and amantadine sensitivity of this construct matches with those observed for other Influenza A M2 constructs in Xenopus oocytes and MEL cells. Similar results were observed in two additional folded-bilayer experiments and further studies are in progress.

505-Pos Board B305
Permeation Properties of CALHM1
Adam P. Siebert, Zhongming Ma, J. Kevin Foskett.
Department of Physiology, University of Pennsylvania, Philadelphia, PA 19104
Recently, CALHM1, a gene of previously unknown function, was identified as a risk factor for late-onset Alzheimer's disease (AD). It was suggested that CALHM1 might be an ion channel or ion channel regulator. We used two-electrode voltage clamp (TEV) to measure CALHM1-induced ionic conductances in the plasma membrane of *Xenopus* oocytes. To investigate which ions permeate the CALHM1-induced conductance, we employed instantaneous current/voltage protocols to measure reversal potentials (E_{rev}) in various solutions. In the absence of extracellular divalent cations, CALHM1 is weakly cation selective, with $P_{Na} : P_K : P_{Cl} = 1 : 1.11 : 0.52$. In CALHM1 injected oocytes, the relative permeability among monovalent cations (with respect to Na^+) is $P_{Rb} = P_{Cs} = P_K > P_{Na} > P_{Li} > P_{NMDG}$, indicating that CALHM1-induced permeability is relatively nonselective for monovalent cations. CALHM1 induced currents are divalent cation selective, with $P_{Na} : P_{Ca} : P_{Ba} : P_{Mg} = 1 : 13.8 : 8.6 : 3.1$. This selectivity sequence represents a Sherry III/IV sequence, consistent with a weak-field strength site in the permeation pore. The presence of extracellular divalent cations strongly alters the gating properties of CALHM1 induced currents. However, the presence of extracellular divalent cations only slightly alters the relative permeability of K^+ and Cl^- ($P_{Na} : P_K : P_{Cl} = 1 : 1.46 : 0.88$). Using large organic cations and a volume exclusion model, we estimated the radius of the CALHM1 associated ion channel pore in the absence of divalent cations to be 6.9 to 8.7 Å. (Supported by NIH GM/DK56328 and a pilot project from the University Pennsylvania AD Core Center.)

506-Pos Board B306
A first Passage Time Analysis of Atomic-Resolution Simulations of the Ionic Transport in a Bacterial Porin
Carles Calero.
We study the transport of potassium and chloride ions and of water through the OmpF porin, a transmembrane nanochannel located at the outer membrane of Escherichia coli. Using the results of extensive all-atom molecular dynamics simulations of the system, we employ a first time passage analysis to understand the transport of ions and water through the channel in terms of a one dimensional biased diffusion model. We explore the applicability of such a description and extract the diffusion coefficients and effective forces characterizing the dynamics of the particles in different regions of the channel. In this analysis, we recognize the appearance of effective entropic forces directed towards the maximization of the available volume of the diffusing particle.

Neuronal Systems & Modeling

507-Pos Board B307
Cerebral Oxygenation During Anesthesia
William Mantulin, Lingzhong Meng.
Cerebral Oxygenation During Anesthesia: Correlation With Blood Pressure and Cardiac Output
William W. Mantulin* and Lingzhong Meng**
University of California Irvine
Beckman Laser Institute,* Laboratory for Fluorescence Dynamics* and Department of Anesthesiology**
Irvine, CA
During surgery, the anesthesiologist is tasked with monitoring, manipulating and maintaining the patient's key physiological parameters, especially of critical organs such as the brain. Generally, cerebral tissue oxygenation is not explicitly tracked, but a measure of Mean Arterial Pressure (MAP) is considered an adequate surrogate marker for sufficient cardiac output to satisfy cerebral oxygen demand. Avoidance of cerebral ischemia is an important consideration. Consequently, we have used a tissue oximeter (Oxipex TS; ISS, Inc.) to non-invasively and quantitatively monitor cerebral oxygenation (bilateral; frontal lobes) during surgery in more than two dozen patients (under IRB approved protocols). If blood pressure declines after inducing anesthesia, then the anesthesiologist pharmacologically intervenes with a pressor such as Ephedrine or Phenylephrine. Phenylephrine acts as a vasoconstrictor, whereas ephedrine stimulates cardiac output. We were intrigued by our preliminary observations that cerebral oxygenation (and oxygenated Hemoglobin concentrations) declined with administration of Phenylephrine, but remained unchanged with Ephedrine. Both pressors produced the anticipated increase in blood pressure. We sought a correlation of this observation through a direct monitor of cardiac output with a Doppler Esophageal device (Cardio Q, Deltex Inc.). The data clearly showed that administration of Phenylephrine induced a decrease in cardiac output and a correlation with (a decreasing) cerebral oxygenation. The cerebral blood volume and tissue oxygen saturation tracked with the blood pressure. Our observations are now engendering a reexamination amongst clinicians as to how best to understand the interplay between cardiac output, mean arterial pressure and the use of increased blood pressure as a means to better perfuse and oxygenate critical organs such as the brain.

508-Pos Board B308
Biophysical Effects of a Novel Biodegradable Copolymer on the Repair of Damaged Neural Membranes
Sogolie Kouhzaei, Hamid Mobasheri.
The pathophysiology of Spinal cord injury (SCI) is involved primary mechanical injury followed by secondary delayed injury. Neural membrane is the most susceptible part of the cell and most of the time mechanical injury results in axolemma disruption and failure to function as an electrical and ionic barrier. This leads to blockage of nerve impulse conduction, deregulation of ionic gradients; free radical associated lipid peroxidation of membrane and increased influx of calcium ions that activates calpain and caspase-dependent cell death cascades. Thus immediate membrane repair can prevent various destructive processes, restoring of the physicochemical balance of the cytoplasm and ultimate functional recovery in neurons. Several degradable polymers and surfactants including PEG, Poloxamer 188, and poloxamine 1107 have shown to be effective in sealing and halting progressive permeabilization. Here, we applied ultrasound wave as mechanical insult to make transient breaches in membrane to simulate membrane damage in SCI and used a novel triblock copolymer of PEG-(fumaric-sebacic acids)-PEG to seal membrane breaches. Cell survival and membrane integrity were checked by MTT assay and Trypan blue exclusion test respectively. The results showed that this copolymer can be a promising candidate for membrane sealing. Now we are assessing the effects of this polymer on *in vivo* spinal cord evoked potential (SCEP).

509-Pos Board B309
Computational Investigation of the Mechanism Behind Sidearm-Mediated Neurofilament Interaction
Lakshmi Jayanthi, William Stevenson, Rakwoo Chang,
Yeshitila Gebremichael.
Neurofilaments (NFs) are essential cytoskeletal filaments that determine the axonal caliber and impart mechanical integrity to the nerve cells. They are assembled from three distinct molecular weight proteins - neurofilament light (NF-L), medium (NF-M), and heavy (NF-H). The three proteins are bound to each other laterally forming 10-nm filamentous rods along with sidearm extensions that vary in the number and sequences of amino acid residues. Additionally, the polypeptide chains attain negative charges through serine phosphorylation of the Lys-Ser-Pro (KSP) repeat motifs that are particularly found in the NF-H and NF-M sidearms. The NF sidearms are known to mediate the interaction between neurofilaments, and a number of models have been proposed in the literature for describing the interfilament interactions. However, the precise mechanism by which NF sidearms regulate NF-NF interaction remains unsettled. To understand the exact nature of sidearm-mediated interactions, we employed the polymer brush model of NF (Chang et al. J. Mol. Biol. (2009) 391:648-660). The model incorporates the stoichiometry and charge distribution of NF sidearms, where the latter arises from the ionizable amino acids as well as the KSP repeat motifs of the polypeptide chains. By using the NF brush model, we performed Monte Carlo simulations to investigate the interaction between neurofilaments under various conditions. We present the analyses of Monte Carlo simulations that are carried out to reveal the underlying mechanism behind interfilament interactions.